

**Amendments to the Claims:**

The listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently amended) A method for identifying a compound that modulates the activity of a T1R or T2R taste receptor by a Gi protein signaling pathway comprising:

i. providing a eukaryotic cell that expresses at least one functional T1R or T2R taste receptor and a G<sub>i</sub> protein that couples thereto;

ii. contacting said eukaryotic cell with at least one compound that putatively modulates the activity of said T1R or T2R;

iii. assaying the effect of said putative modulatory compound on at least one of of MAPK activation , cAMP accumulation or adenylyl cyclase activity in said eukaryotic cell;

iv. identifying whether said at least one putative modulatory compound modulates the activity of such functional T1R or T2R expressed by said eukaryotic cell by a G<sub>i</sub> protein signaling pathway based on its effect on at least one of MAPK activity, cAMP accumulation or adenylyl cyclase activity.

2. (Original) The method of claim 1 wherein said eukaryotic cell is selected from the group consisting of insect cells, amphibian cells, yeast cells, worm cells and mammalian cells.

3. (Currently amended) The method of claim 1 wherein said eukaryotic cell is selected from the group consisting of HEK-293 cells, CHO cells, mouse macrophages, ~~Hela~~ HeLa cells and BHK cells.

4. (Original) The method of claim 1 which is a high throughput screening assay.

5. (Original) The method of claim 1 wherein the assay step (iii) detects activation of MAPK.

6. (Original) The method of claim 5 wherein MAPK activation is detected using a ligand that specifically binds MAPK.

7. (Original) The method of claim 5 wherein said ligand is a monoclonal or polyclonal antibody that specifically binds activated (phosphorylated) MAPK.

8. (Currently amended) The method of claim 6 7 wherein said monoclonal antibody specifically binds phosphorylated p44/42 MAP Kinase (ERK1 or ERK2).

9. (Original) The method of claim 1 wherein said assay step (iii) detects whether said putative modulatory compounds results in a decrease in cAMP accumulation.

10. (Original) The method of claim 9 wherein cAMP accumulation is detected using a ligand that specifically binds cAMP.

11. (Original) The method of claim 9 wherein cAMP levels are detected by a chemiluminescent, radiological or fluourescent immunoassay technique.

12. (Original) The method of claim 9 wherein cAMP accumulation is induced prior to contacting the eukaryotic cell with a putative T1R or T2R modulatory compound.

13. (Original) The method of claim 12 wherein cAMP accumulation is induced by addition of forskolin.

14. (Original) The method of claim 1 wherein said assay step (iii) detects whether said putative modulator inhibits adenylyl cyclase activity.

15. (Original) The method of claim 1 wherein said eukaryotic cell stably expresses said at least one T1R or T2R.

16. (Original) The method of claim 1 wherein said eukaryotic cell transiently expresses said at least one T1R or T2R.

17. (Original) The method of claim 1 wherein said eukaryotic cell stably expresses a  $G_i$  protein that functionally couples to said T1R or T2R.

18. (Cancel)

19. (Original) The method of claim 17 wherein said  $G_i$  protein is selected from the group consisting of [ $G\alpha_{15}$ ,  $G\alpha_{16}$ ,  $G\alpha_{i-1}$ ,  $G\alpha_{i-2}$ ,  $G\alpha_{i-3}$ ,  $G\alpha_{0-1}$ ,  $G\alpha_{0-2}$ , and  $G\alpha_{\alpha z}$ , or variant or a chimera thereof that couples to said at least one T1R or T2R.

20. (Original) The method of claim 17 wherein said eukaryotic cell is transfected with a DNA that encodes said  $G_i$  protein.

21. (Original) The method claim 17 wherein said eukaryotic cell endogenously expresses said  $G_i$  protein.

22. (Original) The method of claim 5 wherein MAPK activation is detected by use of a proximity assay.

23. (Original) The method of claim 10 wherein cAMP accumulation is detected by an immunoassay.

24. (Cancel)

25. (Cancel)

26. (Currently amended) A method for identifying a compound that modulates the effect of another compound on T1R or T2R activity by a  $G_i$  protein signaling pathway comprising the following steps:

i. obtaining a eukaryotic cell that expresses at least one T1R or T2R receptor and a  $G_i$  protein that functionally couples to said T1R or T2R;

ii. contacting said eukaryotic cell with at least one compound that modulates the activity of said T1R or T2R;

iii. further contacting said eukaryotic cell with at least one compound that putatively modulates the effect of said compound in (ii) on T1R or T2R activity;

iv. determining whether said at least one putative modulatory compound in (iii) modulates the effect of said compound (ii) on T1R or T2R activity on a  $G_i$  protein

signaling pathway by measuring the effect of said putative modulator compound (iii) on at least one of MAPK activity, cAMP accumulation, or adenylyl cyclase activity.

27. (Original) The method of claim 26 wherein said eukaryotic cell expresses a functional T1R1/T1R3 umami taste receptor and the compound in (ii) is monosodium glutamate, L-aspartate or L-glutamate.

28. (Original) The method of claim 26 wherein said eukaryotic cell expresses a functional T1R2/T1R3 sweet taste receptor and the compound in (ii) is a natural or artificial sweetener.

29. (Original) The method claim 28 wherein said sweetener is selected from the group consisting of saccharin, glucose, sucrose, sorbitol, xylose, dextran, aspartame, monellin, cyclamate, fructose, and trehalose.

30. (Original) The method claim 26 wherein said eukaryotic cell expresses a functional T2R bitter taste receptor and the compound in (ii) is a bitter compound that activates said T2R.

31. (Original) The method of claim 30 wherein said bitter compound is selected from the group consisting of quinine, denatonium, lidocaine, cycloheximide, strychnine, salicin, and phenylthiocarbamide.

32. (Original) The method of claim 31 wherein said T2R is selected from the group consisting of mT2R5, rT2R9, TAS2R10, TAS2R16, and TAS2R38.

33. (Original) The method of claim 29 wherein said eukaryotic cell endogenously expresses a  $G_i$  protein that couples to said T1R or T2R.

34. (Original) The method of claim 33 wherein said  $G_i$  protein selected is selected from  $G_{\alpha i-1}$ ,  $G_{\alpha i-2}$ ,  $G_{\alpha i-3}$ ,  $G_{\alpha 0-1}$ ,  $G_{\alpha 0-2}$  and  $G_{\alpha z}$  or a variant or chimera thereof that functionally couples to said T1R or T2R.

35. (Original) The method of claim 34 wherein said  $G_i$  protein is a member of the  $G_{\alpha i1-3}$  subfamily.

36. (Original) The method of claim 26 which is used to identify a compound that blocks bitter taste associated with a particular T2R activator.

37. (Original) The method of claim 26 which is used to identify a compound that blocks or enhances umami taste elicited by a compound that activates the T1R1/T1R3 (umami) taste receptor.

38. (Original) The method of claim 37 wherein said compound is a glutamate containing compound.

39. (Original) The method of claim 28 wherein said compound is monosodium glutamate.

40. (Original) The method of claim 26 which is used to identify a compound that blocks or enhances sweet taste elicited by a compound that activates the T1R2/T1R3 (sweet) taste receptor.

41. (Original) The method of claim 40 wherein said compound is an artificial or natural sweetener.

42. (Original) The method of claim 41 wherein said sweetener compound is selected from the group consisting of saccharin, xylitol, sucrose, glucose, cyclamate, monellin, dextran, glucose, xorbitol, fructose, and D- or L-tryptophan.

43. (Original) The method of claim 36 wherein the bitter compound that activates said T2R is selected from the group consisting of quinine, denatonium benzoate, lidocaine, and cycloheximide.

44. (Original) The method of claim 26 wherein in step (iv), the effect of said putative modulator of said compound is detected based on its effect on MAPK activity.

45. (Original) The method of claim 44 wherein MAPK activity is detected by immunoassay.

46. (Currently amended) The method of claim ~~43~~ 45 wherein said immunoassay uses an antibody that specifically binds an activated form of MAPK.

47. (Currently amended) The method of claim 1 wherein said T1R is selected from the group consisting of rat, mice and human T1Rs3.

48. (Original) The method of claim 47 wherein said T1R is selected from the group consisting of mouse, human and rat T1R1, mouse, human and rat T1R2 and mouse, human and rat T1R3.

49. (Original) The method of claim 1 wherein the eukaryotic cell co-expresses T1R1 and T1R3 or co-expresses T1R2 and T1R3.

50. (Original) The method of claim 1 wherein in step (iii) MAPK is assayed by use of a phosphospecific antibody cell-based ELISA (PACE).

51. (Original) The method of claim 1 wherein the eukaryotic cells are cultured in multi-well plates.

52. (Original) The method of claim 1 wherein said eukaryotic cells are adhered to a substrate.

53. (Original) The method of claim 1 wherein said eukaryotic cells are in suspension.

54. (Original) The method of claim 1 wherein the effect of said modulator compound on MAPK activation, cAMP accumulation or adenylyl cyclase activity is concentration (dose) dependent.

55. (Original) An assay kit for the identification of a modulator of a T1R or T2R, wherein said modulator modulates a G<sub>i</sub> protein signaling pathway, that comprises:

i. a eukaryotic cell that stably or transiently expresses at least one T1R or T2R and a G<sub>i</sub> protein that couples functionally thereto;

ii. a ligand or reagent that provides for the detection of an activated form of MAPK, cAMP or adenylyl cyclase.



56. (Original) The assay kit of claim 55 wherein the eukaryotic cell is a yeast, mammalian, insect, amphibian or worm cell.

57. (Currently amended) The assay kit of claim 56 wherein the eukaryotic cell is an HEK-293, BHK, CHO, Xenopus oocyte or ~~Hela~~ HeLa cell.

58. (Currently amended) The assay kit of claim 40 wherein said ligand or reagent is attached to a detectable label.

59. (Original) The assay kit of claim 55 wherein said label is a detectable label is an enzyme, fluorophore, chemiluminescent compound, or radionuclide.

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61. (Cancel)

62. (Cancel)

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